REMARKS

Claims at Issue. Applicant understands claims 1, 3-9 and 15-24 to be at issue. New claims 25 - 27, drawn to a cyclic peptide, are added by amendment.

Claims Rejection - 35 U.S.C. § 101. Claims 1, 17 and 21 have been amended by modifying the word peptide with the adjective "purified."

35 U.S.C. § 112, first paragraph, rejection of Claims 1, 3-9 and 15-24, Written Description. Claims 4, 6 and 21 have each been amended to include the closed language "consisting of". These claims, and dependent claims 22-24, are not subject to rejection on this basis under any written description analysis.

It is submitted that the rejection is not proper under the *Revised Interim Guidelines*. This is particularly true with respect to claims 17 to 20 drawn not to "any" antigen but rather to mRNA encoding a filaggrin or profilaggrin antigen. Under the *Revised Interim Guidelines*, the "written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a), above), reduction to drawings (see (1)(b), above), or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." Here at least ten different species are shown (SEQ ID NO:1 through SEQ ID NO:10). There is no showing on the part of the Examiner that this is not a sufficient representative number of species. Similarly, relevant and identifying characteristics are present in the claim. First, the peptide has 21 or fewer amino acids. Second, the peptide is reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis. Third, the peptide is derived from a contiguous stretch of amino acid residues encoded by mRNA encoding an antigen recognized by autoimmune antibodies in a patient with rheumatoid arthritis. For claim 17, the antigen is limited to mRNA

encoding a filaggrin or profilaggrin antigen. The mRNA must encode at least one arginine residue. At least one arginine residue in the peptide has a modified side chain.

A skilled artisan can clearly envision contemplated peptides by means of the limitations of the claims, and can test them by means of the ELISA and other assays disclosed in the specification.

35 U.S.C. § 112, first paragraph, rejection of Claims 1, 3- 9 and 15-24, Enablement. This ground of rejection is respectfully traversed. The argument with respect to written description is incorporated by reference.

With specific regard to enablement, applicant submits that the Examiner has mistakenly focused solely on "biochemical information" as the grounds for rejection. First, with respect to claims 17 - 20, the sole antigen claimed is filaggrin or profilaggrin. There are an ascertainable and readily identifiable number of peptides of the defined size (21 or fewer amino acids) that are derived from a contiguous stretch of amino acid residues encoded by mRNA for those antigens which contain arginine that has a specific side chain modification and which is reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis. Second, it is noted that Abaza et al. is simply inapposite on the issue of undue experimentation. Abaza et al. is concerned with **monoclonal** antibodies, which are highly specific. However, autoantibodies, such as the autoimmune antibodies of claims 1 and 17, are polyclonal antibodies. Teachings with respect to a "single amino acid difference in an antigen" with respect to monoclonal antibodies are inapplicable to polyclonal antibodies. Third, it is clear that "undue experimentation" would not be required, and that the experimentation required, such as an ELISA assay to determine reactivity, is both known in the art and disclosed in the specification.

35 U.S.C. § 112, second paragraph, rejection of Claims 1, 3-24, Indefinite. The claims have been amended as suggested by the Examiner, and are submitted to not be indefinite as amended.

Claims 4 and 21-24 rejected under 35 U.S.C. § 102(a) as anticipated by Schellekens et al. It is asserted that "[c]losed language would over this rejection." Claims 4 and 21 have been so amended.

Claims 1, 2-4, 8, 21-22 and 24 rejected under 35 U.S.C. § 102(b) as anticipated by Simon et al. as evidenced by WO/99/35167. Claims 4 and 21 are amended to include closed language. It is accordingly asserted that claims 4, 21-22 and 24 are no longer subject to rejection on this ground, in that the referenced teachings do not disclose peptides with the disclosed sequences or peptides containing the disclosed sequences.

At most, Simon et al. simply teaches that the native filaggrin protein is detected by rheumatoid arthritis-specific autoantibodies. There is no characterization of the epitope or antigen other than to isolate it to the human epidermal protein filaggrin. The Examiner then applies a later reference, by the same research group, as evidence that "the claimed functional limitations would be inherent properties of the referenced peptides." This argument necessarily fails both legally and factually.

The claims, as amended, are drawn to a purified peptide of about 21 or fewer amino acid residues. There is no teaching in Simon et al. of a purified peptide of this length. Simon merely teaches a 40 kD protein, presumably containing somewhere between about 250 and 400 amino acid residues. The appropriate standard for anticipation requires that the elements be described in a single prior art reference. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)." Had Simon et al. taught a purified peptide of about 21 or fewer amino acid residues that inherently and necessarily contained a modified arginine residue, such as citrulline, the rejection might have merit. However, Simon et al. taught only a 40 kD protein, identified as filaggrin. Applicant is not claiming the 40 kD protein. Applicant's invention, as claimed, is a purified peptide with specific limitations that clearly exclude a 40 kD protein.

Ex parte Gray, 10 U.S.P.Q. 2d 1922 (Bd. Pat. App. & Interf., 1989) does not support the position urged by Examiner. In *Ex parte Gray*, the issue was whether human nerve growth factor beta-NFG identified by a particular amino acid sequence was inherently disclosed in prior art references, and thus was unpatentable under 35 U.S.C. § 103. However, it was clear that "the difference between the material of [the prior art] and that claimed by appellants herein resides in the method of obtaining the human growth factor. The prior art material is recovered from natural sources and purified, while appellants' is produced by recombinant DNA methodology." 10 U.S.P.Q.2d at 1924. Thus the invention claimed by appellants and the prior art material was identical -- of the same amino acid composition, molecular weight and the like. By contrast, in this case the prior art discloses only a 40 kD protein, while applicant claims a peptide of much smaller length with a modified arginine residue. The requirement of *Ex parte Gray* and other cases that "the claimed and prior art products [be] identical or substantially identical" (see, e.g., *In re Best*, 562 F.2d 1252,195 U.S.P.Q. 430, 433-434 (CCPA 1977) is not met in this case.

Claims 1, 3-4, 7-9, and 15-24 rejected under 35 U.S.C. § 102(e) as anticipated by Serre et al., U.S. Patent 5,888,833. Applicant respectfully traverses this rejection. For a rejection under 35 U.S.C. § 102(e), the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). See generally MPEP § 2131 *et seq.*

With respect to claims 4 and 21-24, the rejection is clearly improper because Serre et al. does not disclose SEQ ID NO:1 through SEQ ID NO:9. Indeed, Serre et al. discloses no amino acid sequences, and discloses no specific amino acid residues.

With respect to claims 1, 3, 7-9, and 15-20, there is no disclosure in Serre et al. of a modified arginine residue, such as citrullin. A modified arginine residue is an essential element of independent claims 1 and 17. Serre et al. does not even disclose a particular epitope; indeed, the disclosure at col. 6, line 22 bridging col. 7, line 37 makes it clear that multiple epitopes are involved, with the relevant proteins identified and identifiable only to the extent of a "fractionation" technique such as electrophoresis, chromatography or electric focusing. See also cols. 23 and 24, where characterization of the antigen is only at the protein level. Particularly given the clear teaching of Serre et al. that multiple epitopes are present in the identified proteins, there is no scientific or logical basis to assert that the peptides claimed by applicant (i.e., containing a specifically modified arginine residue) are even included with the antigens identified in Serre et al. Put another way, given the disclosure of Serre et al. it is entirely possible that the epitopes discovered by Serre et al. and recognized by autoantibodies are, for example, conformationally dependent structures (e.g., involving specific turns with amino acids or sequences thereof from different portions of the protein forming a receptor). Thus the epitopes of Serre et al. may well not even be isolatable as a peptide.

For there to be anticipation, there must be "identity of invention". *Minnesota Mining and Manufacturing Co. v. Johnson & Johnson Orthopedics, Inc.* 976 F.2d 1559, 1565, 24 USPQ2d 1321, 1326 (Fed. Cir. 1992). That is, anticipation requires that "each element of the claim in issue is found...in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice." *Id.* Serre et al. fail to anticipate the invention as claimed. There is no teaching or suggestion in Serre et al. that a peptide is derived from a contiguous stretch of amino acid residues encoded by mRNA, where the mRNA includes a codon for at least one arginine residue, and where at least one arginine residue has specific and defined side chain modifications.

Conclusion. In view of the above amendments and remarks, it is respectfully submitted that all grounds of rejection and objection have been avoided and/or traversed. It is believed that the case is now in condition for allowance and same is respectfully requested.

If any issues remain, or if the Examiner believes that prosecution of this application might be expedited by discussion of the issues, she is cordially invited to telephone the undersigned attorney for Applicants at the telephone number listed below.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached paper is captioned "**Version with Markings to Show Changes Made**."

Authorization is given to charge payment of any fees required, or credit any overpayment, to Deposit Acct. 13-4213. A duplicate of this paper is enclosed for accounting purposes.

Respectfully submitted,

Dated: November 27, 2002

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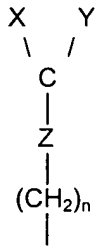
Version with Markings to Show Changes Made

1. (Three Times Amended) A purified peptide [of] consisting of about 21 or fewer amino acids, reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis, wherein the peptide is derived from a contiguous stretch of amino acid residues encoded by mRNA encoding an antigen recognized by autoimmune antibodies in a patient with rheumatoid arthritis, said mRNA comprising a codon for at least one arginine residue, wherein at least one arginine residue in the peptide comprises a modified arginine residue with a side chain of the formula:



wherein

X is NH_2, CH_3, $NHCH_3$ or $N(CH_3)_2$;

Y is O, NH, $NHCH_3$ or $N(CH_3)_2$;

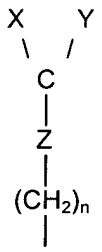
Z is O, NH or CH_2; and

n is 2, 3 or 4, on the condition that when X = NH_3 and Z = NH, Y is not NH.

4. (Five Times Amended) A peptide according to claim 1 wherein the peptide [comprises] consists of a linear peptide selected from the group of peptides consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 and SEQ ID NO:9.

6. (Three Times Amended) A peptide according to claim 5 wherein the cyclic peptide [comprises] consists of SEQ ID NO 10.

17. A purified peptide [of] consisting of about 21 or fewer amino acids reactive with autoimmune antibodies from a patient suffering from rheumatoid arthritis, wherein the peptide is derived from a contiguous stretch of amino acid residues encoded by mRNA encoding a filaggrin or profilaggrin antigen, the mRNA comprising a codon for at least one arginine residue, wherein at least one arginine residue in the peptide comprises a modified arginine residue with a side chain of the formula:



wherein

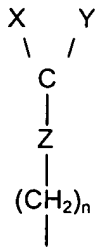
X is NH_2, CH_3, $NHCH_3$ or $N(CH_3)_2$;

Y is O, NH, $NHCH_3$ or $N(CH_3)_2$;

Z is O, NH or CH_2; and

n is 2, 3 or 4, on the condition that when X = NH_3 and Z = NH, Y is not NH.

21. (Twice Amended) A purified peptide [with an] consisting of amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:10, wherein X therein is a modified arginine residue with a side chain of the formula:



wherein

X is NH_2, CH_3, $NHCH_3$ or $N(CH_3)_2$;

Y is O, NH, $NHCH_3$ or $N(CH_3)_2$;

Z is O, NH or CH_2; and

n = 2, 3 or 4, on the condition that when X = NH_3 and Z = NH, Y is not NH.